Thus, despite Katsnelson's interesting model for testing arsenic for carcinogenicity and his findings of a few unusual application–site gastric tumors, we remain unconvinced that the collective experimental findings on arsenic can be taken as proof that arsenic is carcinogenic to animals; by this we mean, on the singular basis of the available animal data (and, for the moment, ignoring the human data), that neither IARC nor the National Toxicology Program (NTP) would judge arsenic as a "probable" or "reasonably anticipated" human carcinogen. The available animal data alone simply do not meet the criteria for either IARC or the NTP to consider the laboratory evidence as being adequate and sufficient to list arsenic as a likely carcinogen to humans. Of course, both organizations do consider arsenic and arsenic compounds as being unequivocally carcinogenic to humans based on epidemiological data.

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References

1. Katsnelson BA, Neizvestinova EM, Blokhin VA. Stomach carcinogenesis induction by chronic treatment with arsenic [in Russisn]. Vopr Onkol 32:68–73 (1986).
2. IARC. Arsenic. In: . IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Supplement 7: Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs 1 to 42. Lyon:International Agency for Research on Cancer, 1987;100–106.
3. Chan P, Huff JE. Arsenic carcinogenesis in animals and in humans: mechanistic, experimental, and epidemiological evidence. Environ Carcinogen Ecotoxicol Rev C15(2):83–122 (1997).
4. IARC. Arsenic and arsenic compounds. In: IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Vol 23: Some Metals and Metallic Compounds. Lyon:International Agency for Research on Cancer, 1980;39–141.
5. Lee TC, Oshimura M, Barrett JC. Comparison of arsenic-induced cell transformation, cytotoxicity, mutation and cytogenetic effects in Syrian hamster embryo cells in culture. Carcinogenesis 6(10): 1421–1426 (1985).
6. Lee TC, Tanaka N, Lamb PW, Gilmer TM, Barrett JC. Induction of gene amplification by arsenic. Science 241(4861):79–81 (1988).
7. NTP. Arsenic and certain arsenic compounds. In: First Report on Carcinogens. Research Triangle Park, NC:National Toxicology Program, 1980;12–13.
8. NTP. Benzene. In: First Report on Carcinogens. Research Triangle Park, NC:National Toxicology Program, 1980;15–16.
9. IARC. Benzene. In: IARC Monographs on the Evaluation of Carcinogenics to Humans. Vol 29: Some Industrial Chemicals and Dyestuffs. Lyon:International Agency for Researc h on Cancer, 1982;93–148.
10. Maltoni C, Scarnato C. First experimental demonstration of the carcinogenic effects of benzene; long-term bioassays on Sprague-Dawley rats by oral administration. Med Lav 70(5):352–3577 (1979).
11. Maltoni C, Ciliberti A, Cotti G, Conti B, Belpoggi F. Benzene, an experimental multipotential carcinogen: results of the long-term bioassays performed at the Bologna Institute of Oncology. Environ Health Perspect 82:109–124 (1989).
12. Huff JE, Haseman JK, DeMarini DM, Eustis S, Maronpot RR, Peters AC, Persing RL, Chrisp CE, Jacobs AC. Multiple-site carcinogenicity of benzene in Fischer 344 rats and B6C3F$_1$ mice. Environ Health Perspect 82:125–163 (1989).
13. Tomatis L. The predictive value of rodent carcinogenicity tests in the evaluation of human risks. Annu Rev Pharmacol Toxicol 19:511–530 (1979).
14. Huff J. Chemicals and cancer in humans: first evidence in experimental animals. Environ Health Perspect 100:201–210 (1993).
15. Tomatis L, Aitio A, Wilbourn J, Shuker L. Human carcinogens so far identified. Jpn J Cancer Res 80(9):795-807 (1989).
16. Huff JE. Chemicals causally associated with cancers in humans and in laboratory animals: a perfect concordance. In: Carcinogenesis (Waalkes MP, Ward JM, eds). New York:Raven Press,. 1994;25–37.
17. Huff JE. Carcinogenesis results in animals predict cancer risks to humans. In: Maxcy-Rosenau-Last's Public Health & Preventive Medicine (Wallace RB, ed). 14th ed. Norwalk, CT:Appleton & Lange, 1998;543–550, 567–569.
18. NTP. Arsenic and certain arsenic compounds. In: Eighth Report on Carcinogens. Research Triangle Park, NC:National Toxicology Program, 1998;17–19.
19. Laib RJ, Moritz H. Investigation of tumor initiating and/or cocarcinogenic properties of arsenite and arsenate with the rat liver foci bioassay. Exp Pathol 37(1–4):231–233 (1989).
20. Thorgeirsson UP, Dalgard DW, Reeves J, Adamson RH. Tumor incidence in a chemical carcinogenesis study of nonhuman primates. Regul Toxicol Pharmacol 19(2):130–151 (1994).
21. Yamamoto S, Konishi Y, Matsuda T, Murai T, Shibata MA, Matsui-Yuasa I, Otani S, Kuroda K, Endo G, Fukushima S. Cancer induction by an organic arsenic compound, dimethylarsinic acid (cacodylic acid), in F344/DuCrj rats after pretreatment with five carcinogens. Cancer Res 55(6):1271–1276 (1995).
22. Germolec DR, Spalding J, Boorman GA, Wilmer JL, Yoshida T, Simeonova PP, Bruccoleri A, Kayama F, Gaido K, Tennant R, et al. Arsenic can mediate skin neoplasia by chronic stimulation of keratinocyte-derived growth factors. Mutat Res 386(3):209–218 (1997).
23. Huff J, Chan P, Waalkes M. Arsenic carcinogenicity testing. Environ Health Perspect 106:A170 (1998).

Independent Review of Industry-generated Data

The commentary of Gibson et al. (*1*) of Dow AgroSciences takes issue with our estimates of potential risks to children from indoor broadcast uses of chlorpyrifos (*2*) that were derived from a recent study by Gurunathan et al. (*3*) at the Environmental and Occupational Health Sciences Institute (EOHSI) of Rutgers University. Specifically, the Dow AgroSciences researchers claim that potential indoor exposures of chlorpyrifos are "approximately 10 times below" those found in the EOHSI study.

Unfortunately, there is no easy way to examine the claim made by Gibson et al. (*1*) because most of the pertinent data on which their statement is based are not available in the peer-reviewed, published literature. Thus, we are unable to determine whether the test protocols or exposure time periods used in the previous unpublished Dow studies are comparable to the experimental approaches used in the EOHSI study. For example, Gibson and colleagues' citation of biomonitoring data of volunteers (simulating childlike activities) following broadcast spraying of chlorpyrifos—demonstrating potential childhood exposures to be 10-fold below EOHSI estimates—is based entirely on one internal, unpublished Dow Chemical Company study (*4*). Similarly, Dow AgroSciences' exposure study after "crack and crevice" treatment by chlorpyrifos for insect infestation is based on an industry-sponsored study whose results were only recently published (*5*).

On the other hand, Gurunathan et al. (*3*) presented a detailed and well-conducted assessment of exposures to chlorpyrifos over a 2-week period following a one-time broadcast application of chlorpyrifos by a licensed pesticide applicator. Most published studies in the past that examined exposure levels related to broadcast spraying of chlorpyrifos did not measure the pesticide's indoor concentration beyond 1 or 2 days following applications [for example, see Fenske et al. (*6*)]. What the EOHSI study showed was that chlorpyrifos, like other semiviolatile pesticides, did not dissipate or settle down, but continued to vaporize into the gas phase and resettle on a variety of solid surfaces indoors (such as children's toys) over an extended period of time.

Furthermore, the experimental protocols used in the EOHSI study (*3*) simulated conditions that may easily lead to an underestimation of exposure to indoor uses of chlorpyrifos. As we stated in our commentary (*2*), in a number of facilities where many children are present

> . . . such as day care centers, schools, and homes, where chlorpyrifos-based products may be frequently sprayed on to control insect infestations, there can be cumulative exposures that are much higher than those currently estimated from the [EOSHI] and other pesticide exposure studies based on single [broadcast] applications.

This exchange raises two pressing issues for public policy. First, those in the public and private sectors charged with developing national guidelines and standards to protect children from environmental hazards often make decisions based on incomplete information. Secondly, we agree with Gibson et al. (*1*) that a weight-of-evidence approach is the best way to resolve issues involving the safety of widely used compounds such as chlorpyrifos.

However, a weight-of-evidence approach can only work if there is full disclosure of industry-generated unpublished studies. In order to obtain scientific consensus on such matters, we propose that technical reviews of unpublished industry data be carried out by scientists and other technical experts working under the aegis of institutions such as the National Academy of Sciences, the Health Effects Institute, or other similar independent organizations. We would welcome the creation of such institutional arrangements to make it possible for exposure and health risk assessments to be conducted on a complete scientific knowledge base.

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References

1. Gibson JE, Peterson RKD, Shurdut BA. Human exposure and risk from indoor use of chlorpyrifos. Environ Health Perspect 106:303–306 (1998).
2. Davis DL, Ahmed AK. Exposures from indoor spraying of chlorpyrifos pose greater health risks to children than currently estimated. Environ Health Perspect 106:299–301 (1998).
3. Gurunathan S, Robson M, Freeman N, Buckley B, Roy A, Meyer R, Bukowski J, Lioy P. Accumulation of chlorpyrifos on residential surfaces and toys accessible to children. Environ Health Perspect 106:9–16 (1998).
4. Vaccaro JR, Nolan RJ, Hugo JM, Pillepich JL, Murphy PG, Bartels MJ. Evaluation of Dislodgeable Residues and Absorbed Doses of Chlorpyrifos to Crawling Infants Following Indoor Broadcast Applications of Chlorpyrifos-based Emulsifiable Concentrate. DECO-HEH2.1-1-182(95). Unpublished Research Report of the Dow Chemical Company, 1991.
5. Byrne S, Shurdut BA, Saunders DG. Potential chlorpyrifos exposure to residents following crack and crevice treatment. Environ Health Perspect 106:725–731 (1998).
6. Fenske RA, Black KG, Elkner KP, Lee CL, Methner MM, Soto R. Potential exposure and health risks of infants following indoor residential pesticide applications., Am J Public Health 80:689–693 (1990).

EMF Working Group

A brief note on the results of the NIEHS EMF working group was given in the September issue of *EHP* [106:A431 (1998)]. It may be helpful if more details of the NIEHS EMF working group deliberations are provided.

The NIEHS EMF working group members voted according to guidelines used in the International Agency for Research on Cancer (IARC) *Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans.* No members voted to classify EMFs as either a known or probable human carcinogen (IARC groups 1 and 2A), 19 members voted to classify EMFs as a possible human carcinogen (IARC group 2B), 8 voted to classify EMFs as not a human carcinogen (IARC group 3), and 1 voted to classify EMFs as probably not a human carcinogen (IARC group 4).

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"Politically Correct" Research

It is unfortunate that the National Institutes of Health have become so politicized. I do not understand how the original study of Swan et al. [Have Sperm Densities Declined? A Reanalysis of Global Trend Data. *EHP* 105:1228–1232 (1997)] got such widespread attention; one would expect the arguably most important government organ concerned with the study of health issues in the United States to have a higher standard than that exemplified in its dissemination of its original study.

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